REMARKS/ARGUMENTS

All of the claims of this application, namely claims 1-46, have been rejected under 35 U.S.C. §103(a) as being unpatentable over Stainmesse et al. U.S. Patent No. 5,133,908 (Stainmesse) in view of Cima et al. U.S. Patent Application Publication No. 2002/0048610 (Cima). Furthermore, all claims have been rejected under the doctrine of obviousness-type double patenting over Claims 1-108 of U.S Patent No. 6,607,784; Claims 1-99 of U.S. Patent No. 6,869,617; Claims 1-84 of U.S. Patent No. 6,951,656; and Claims 1-97 of U.S. Patent 6,884,436. In addition, the Examiner rejected the Claims of the pending application under the doctrine of provisional obviousness-type double patenting over the allowed Claims 1-15 and 18-21 of copending application No. 09/874,499 (now U.S Patent No. 7,037,528) and Claims 1-108 of copending application No. 10/246,802.

In this response to the Office Action, the Claims have not been amended.

Rejection under USC 103(a): Stainmesse and Cima

The Examiner argues that Stainmesse teaches methods of producing nanoparticles comprising: first, preparing a liquid phase consisting essentially of a solution of the substance in a solvent or in a mixture of solvents to which one or more surfactants may be added; the preparation of a second liquid phase consisting essentially of a non-solvent or a mixture of non-solvents for the substance to which one or more surfactants may be added, the non-solvent or the mixture of non-solvents for the substance being miscible in all proportions with the solvent or mixture of solvents for the substance; and third the addition of one of the liquid phases prepared in the first or second step to the other with moderate stirring so as to produce a colloidal suspension of nanoparticles of the substance; and fourth if desired, the removal of all or part of the solvent or the mixture of solvents for the substance and of the non-solvent or the mixture of non-solvents for the substance so as to give rise to a colloidal suspension of nanoparticles of the desired concentration or to lead to a powder of nanoparticles.

However, in contrast to Applicants' disclosure and claims (e.g. see independent claims 1, 45 and 46), Stainmesse does not teach the use of homogenization for the preparation of small

particles. In fact, Stainmesse teaches away from the use of equipment such as homogenizers for the industrial production of particles of a substance(see Column 1, lines 56-59). In the current application, Applicants claim methods that use homogenization in the processing of particles. As indicated throughout the application, homogenization provides one means to add energy to the process of producing particles. Homogenization may serve several purposes including but not limited to stabilizing particles, reducing particle size, and seeding. Furthermore, all Applicants' claims call for simultaneous homogenization and solvent removal. In Claim 46, homogenization and solvent removal occur simultaneously with mixing.

In the current application, Applicants have developed combined and continuous processes for producing particles (described in paras [105-117], FIGs. 18-22 and Examples 19-25). In one embodiment, homogenization of the mix can be performed simultaneously with the continuous removal of solvent (Independent Claim 1 and Claim 45). In another embodiment, homogenization of the mix is performed simultaneously with the continuous removal of solvent by cross-flow ultra-filtration (Independent Claim 45). In a further embodiment, the mixing of

the solution and the second solvent occurs simultaneously with homogenization and the continuous removal of solvent (Claim 46). As Applicants indicate, these combined and continuous processes have numerous advantages for the industrial scale production of particles (e.g. see paragraphs [105]-[117]). For example, removal of solvent simultaneously with homogenization reduces Ostwald ripening. Stainmesse does not address or even recognize the simultaneous use of homogenization and solvent removal by methods such as filtration. Stainmesse teaches the optional removal of solvent only after the production of particles using lyophilization or evaporation.

Similarly, Cima does not teach the use of homogenization in the production of particles. Cima is directed to methods for generating different forms of crystals of a particular compound and then screening with the goal of identifying forms that have desirable properties. Cima teaches away from physical processing of crystals after crystal formation. For example, Cima states that milling of crystals leads to amorphization (see bottom of paragraph [0025]). In one embodiment of Cima, the crystals are grown in multiwell dishes and then analyzed using a number of assays. The publication states that the methods are done on a small scale, typically less than 1 g (see paragraph

[0170]). Cima does not describe combined and continuous processes where particle size, particle aggregation and solvent removal, amongst other parameters, can be adjusted easily for the large scale production of particles as in Applicants' claimed methods. Cima does mention Ostwald ripening of crystals but does not describe methods to address it.

As the Examiner notes, Cima discloses various method steps to produce crystals. Seeding is one method that can be used to generate different crystal forms. It is Applicants' disclosure, not Cima, that teaches homogenization as one method that can be used to perform seeding. Cima does not teach the use of homogenization to perform seeding and, indeed, **does not mention homogenization at all.**

It is respectfully observed that the combination of Stainmesse and Cima would not obviously lead one of ordinary skill in the art to the presently claimed methods. This combination of references does not suggest the methods in the present application which provide important advantages in the formation of particles.

Obviousness Double-Patenting Rejection

The Examiner states that the Claims of U.S. Patent Nos. 6,607,784; 6,869,617; 6,951,656; and 6,884,436 as well as Application Nos. 09/874,499 (now U.S. Patent No. 7,037,528) and 10/246,802 are substantially drawn to processes for preparing submicron-sized particles, which involves dissolving an organic compound in a water-miscible first solvent, mixing the resulting solution with a second solvent to define a pre-suspension, and adding energy to the mixture. Applicants respectfully suggest that the claims of the current Application are patentably distinct from the claims of those patents and applications. Nevertheless, Applicants submit a Terminal Disclaimer.

Reconsideration and withdrawal of the double-patenting rejection is respectfully requested, as is the allowance of the present application.

Respectfully submitted,

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